

Leading article

Nomenclature of TEM β -lactamasesKaren Bush^a and George Jacoby^b^aAstra Research Center Boston, Cambridge, MA 02139-4239; ^bLahey Hitchcock Clinic, Burlington, MA 01805, USA

β -Lactamase nomenclature has never been particularly rational. Enzymes have been named after a preferred substrate (CARB, FUR, IMP, OXA), other biochemical properties (SHV, NBC), genes (Amp, CepA), bacteria (AER, PSE), strains (P99), patients (TEM, ROB), hospitals (MIR, RHH), states (OHIO) and from the initials of their authors (HMS). A particular issue has arisen with the proliferation of naturally occurring TEM derivatives (Table). TEM-1 and TEM-2 are biochemical twins differentiated by isoelectric point and now known to vary by substitution of lysine for glutamine at position 39. TEM-13 resembles TEM-2 with a functionally silent methionine for threonine substitution at position 265. The other TEM enzymes listed in the Table either have an extended spectrum of hydrolysis, and hence are variably active on oxymino- β -lactam substrates such as aztreonam, cefotaxime, ceftazidime and ceftriaxone (TEM-3 to -12, TEM-16 to -29 and TEM-42 and -43), or are resistant to inhibition by agents such as clavulanate, sulbactam and tazobactam (TEM-30 to -41). Missing TEM numbers (TEM-14 and 15, TEM-17 to -19, TEM-22 and TEM-23) either have yet to be fully sequenced or have been shown to be identical in amino acid sequence to others in the list.

Before their defining alterations were known, many of these enzymes were given temporary but descriptive names such as CAZ-1 or CTX-1 to emphasize a preferred substrate (ceftazidime or cefotaxime, respectively) or, for example, IRT-2 to highlight an inhibitor-resistant TEM. This served a useful purpose by defining a functional characteristic of the enzyme. After the sequence was known, a TEM number was then assigned. The use of TEM numbers is now preferred because assignment of phenotypic names can be subjective. How rapidly must ceftazidime be hydrolysed in order to name an enzyme a 'CAZ' β -lactamase? What differential in activity is required for a 'CTX' designation rather than 'CAZ' for an enzyme that hydrolyses both substrates? How much must a K_i or an IC_{50} value be increased for an enzyme to be an 'IRT'? These criteria can be, and are, defined differently by individual groups.

Since those working outside the β -lactamase field may legitimately argue that there are already too many names for β -lactamases, we urge that TEM derivatives be simply given a TEM number and not a further descriptive name. Granted that a TEM number cannot convey a particular phenotype, a descriptive phrase can easily be added where necessary, such as 'extended-spectrum β -lactamase (ESBL) TEM-26' or 'inhibitor-resistant β -lactamase (IRBL) TEM-35'. Sequencing the gene of a novel β -lactamase to establish that it is unique has become almost routine and, if a new sequence is found, there is no need for a descriptive title other than a TEM number.

To qualify for a new TEM number the amino acid sequence of the native enzyme and not just the nucleotide sequence should be unique. Nucleotide substitutions that are functionally silent may be instructive concerning the derivation of a *bla* gene, but they cannot, by definition, encode a new β -lactamase. Similarly, a change in the promoter sequence does not define a new enzyme variety, and amino acid substitutions in the signal sequence (the first 23 amino acids at the NH₂-terminus) that is removed to yield active enzyme should not by themselves define a unique TEM number. An amino acid alteration, even if, currently, no functional change is evident, does qualify since an effect on interaction with a future substrate or inhibitor is always possible. We further propose that TEM numbers should be assigned sequentially independently of the properties of the enzyme, a necessary condition since the TEM number of the latest extended-spectrum enzymes (TEM-42 and -43) already overlap with the numbers of inhibitor-resistant TEM enzymes (Table).

Although it has been suggested that blocks of numbers be reserved for future extended-spectrum and inhibitor-resistant TEMs, this approach will not be viable when an inhibitor-resistant extended-spectrum TEM is discovered. Already TEM-43 has mutations found in both types of TEM variants, and even more combinations of mutations can be expected in the future.

In conclusion, we strongly advocate the use of the TEM numbering system for all β -lactamases related

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Table. Defining amino acid substitutions of β -lactamases

β -Lactamase	Alternative name(s)	Amino acid ^a at position																pI	Reference
		21	39	42	69	104	153	164	165	182	237	238	240	244	265	275	276		
TEM-1	RTEM-1	L	Q	A	M	E	H	R	W	M	A	G	E	R	Y	R	N	5.4	3
TEM-2			K									S						5.6	3
TEM-3	CTX-1		K		K	K						S			M			6.3	3
TEM-4		P									T							5.9	3
TEM-5	CAZ-1							S					K					5.6	3
TEM-6						K		H										5.9	3
TEM-7			K					S				S						5.4	3
TEM-8	CAZ-2		K			K		S						M				5.9	3
TEM-9	RHH-1	P	K		K	K		S										5.6	3
TEM-10	MGH-1, TEM-E3							S					K					5.6	3
TEM-11	CAZ-10		K					H				?						5.25	5
TEM-12	YOU-2, CAZ-3, TEM-E2		K					S						M				5.6	3
TEM-13			K															6.3	3
TEM-16	CAZ-7		K			K		H				S						5.4	1
TEM-20																		6.4	1
TEM-21						K	R	S		T		S						6.5	3
TEM-24	CAZ-6		K			K							K		M			5.3	3
TEM-25	CTX-2	P				K												5.6	3
TEM-26	YOU-1							S					K		M			5.9	6
TEM-27								H					K					6.1	2
TEM-28																		5.42	1
TEM-29														S				5.2	3
TEM-30	IRT-2, TRI-2, E-GUBR													C				5.2	3
TEM-31	IRT-1, TRI-1, E-SAL									T								5.4	4
TEM-32	IRT-3				I													5.4	3
TEM-33	IRT-5				L													5.4	3
TEM-34	IRT-6				V													5.4	3
TEM-35	IRT-4				L													5.2	3
TEM-36	IRT-7				V													5.2	3
TEM-37	IRT-8				I													5.2	4
TEM-38	IRT-9				V													5.4	4
TEM-39	IRT-10				L													5.4	8
TEM-40	IRT-167				I				R									5.2	8
TEM-41			K	V														5.8	7
TEM-42						K		H		T		S	K		M			6.1	9
TEM-43																			

^a Abbreviations: A, alanine; D, aspartic acid; E, glutamic acid; G, glycine; H, histidine; I, isoleucine; K, lysine; L, leucine; M, methionine; N, asparagine; P, proline; Q, glutamine; R, arginine; S, serine; T, threonine; V, valine; W, tryptophan; ?, unknown.

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closely to TEM-1. To avoid inadvertent duplications, a listing of current designations for TEM and other β -lactamases such as SHV and OXA-types will soon be maintained on the Internet linked to <http://www.asmusa.org> and application can be made to the authors for a new listing.

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JAC

Editorial

Changes to Journal Design

Martin J. Wood

Editor-in-Chief

Readers will notice significant changes in the design of *The Journal of Antimicrobial Chemotherapy*, beginning with this issue. These changes have been made because it was felt by many that the layout that had remained largely unchanged for the first 21 years was looking tired and dated. At the same time, we were well aware that, over the years, JAC had established a distinctive visual style. Hence, in these changes, we have attempted to make the Journal look less dull while maintaining its scientific authority and the most characteristic elements of its style.

The most obvious change is to the size of the pages. Very few medical journals still publish in B5 format and,

whereas there may be merit in standing out from the crowd, we believe that the change to 'American' A4 will help open up the text and make it less forbidding. Two other changes will also contribute to our achieving this objective. The first is the adoption of two columns of text for the body of the articles and the references and the second is the citation of those references in a numerical style within the text. This change from a 'Harvard'-based to a 'Vancouver' (numerical citation)-based system was one of the more difficult decisions and we are resigned to the fact that not all our readers will approve. Perhaps those that do not will be relieved by the decision to retain the style of reference listing, punctuation and all!